BioRisk 12: 1–23 (2017)
doi: 10.3897/biorisk.12.12156
www.pensoftonline.net/biorisk

REVIEW ARTICLE

A peer-reviewed open-access journal
BioRisk

Global Trends in Biorisk Management

Sreenivas Reddy Bathula[1,2], A. Rakhimol[1]

1 *Department of Biotechnology, Bapuji Institute of Engineering and Technology, Davanagere - 577004, Karnataka, India* **2** *SAVI EASY LIFE s.r.o., Praha 5, 15000, Czech Republic*

Corresponding author: *Sreenivas Reddy Bathula* (jaishwa@hotmail.com)

Academic editor: *J. Spangenberg* | Received 7 February 2017 | Accepted 17 June 2017 | Published 14 July 2017

Citation: Bathula SR, Rakhimol A (2017) Global Trends in Biorisk Management. BioRisk 12: 1–23. https://doi.org/10.3897/biorisk.12.12156

Abstract

This report recapitulates the diverse aspects of biological safety. Biological laboratory is a space that facilitates the handling and storage of microorganisms, their components or their derivatives. Laboratories that handle dangerous pathogens have to act in a responsible manner to manage the safety and security threats posed by these pathogens. This necessity was foreground in the December 2008 World at risk report, which specifically demanded bioscience laboratories that handle dangerous pathogens to implement a unified laboratory biorisk management framework to enhance their safety and security. The report also discusses the guidelines of biosafety regulations provided by World Health Organization (WHO) that are necessary to adequately and sustainably manage these biorisks and helps in better understanding of risk governance approaches for laboratories that handle dangerous pathogens to achieve the ultimate goal of minimizing or preventing the occurrence and consequences of human error within the laboratory environment: the biorisk management approach, composed of biosafety, laboratory biosecurity and ethical responsibility. It preferably provides an agreement between authorities, the public, and the scientific community establishing trust and societal safety and security, while enabling the continued progress of science. Biorisk management approach demonstrates that biorisks in all their potential forms are appropriately addressed, managed and minimized. Thus, biorisk management has become an important aspect of the development and sustainability of biological activities.

Keywords

Biorisk, Biosafety, biosecurity, biosafety level laboratories and laboratory management

Introduction

Management of biological safety and security risks is a difficult and costly venture. It requires a comprehensive system incorporating the most important aspects of biorisk which encompasses both policy and management aspects. Biorisk governance aims at providing a framework for an organization to enable biorisk assessment and biorisk management activities to take place in a sustainable way. It not only improves decision making, planning and prioritisation, but also contributes to a more efficient allocation and use of the valuable biological materials (VBM) within a laboratory. Biorisk management, thus creates value by ensuring that the resources are efficiently used and thus guarantee the achievement of the strategic objectives (Fig. 1).

Biorisk governance is based on detailed risk assessment, sound decision making, strict and consistent implementation of appropriate risk mitigation measures, monitoring and reviewing (Fig. 2).

Biorisk assessment forms the basis of biorisk management. Biological risk assessment is a legal obligation in many countries that have biosafety regulations, as part of the notification or authorization process and/or as a basis to determine the required containment levels and other protective or preventive measures. It is also a major element of the WHO laboratory biosafety manual and a basis of the laboratory biorisk management standard CWA 157937.

Biosafety and biosecurity are the two components of biorisk (WHO 2004).

Figure 1. AMP model of biorisk management.

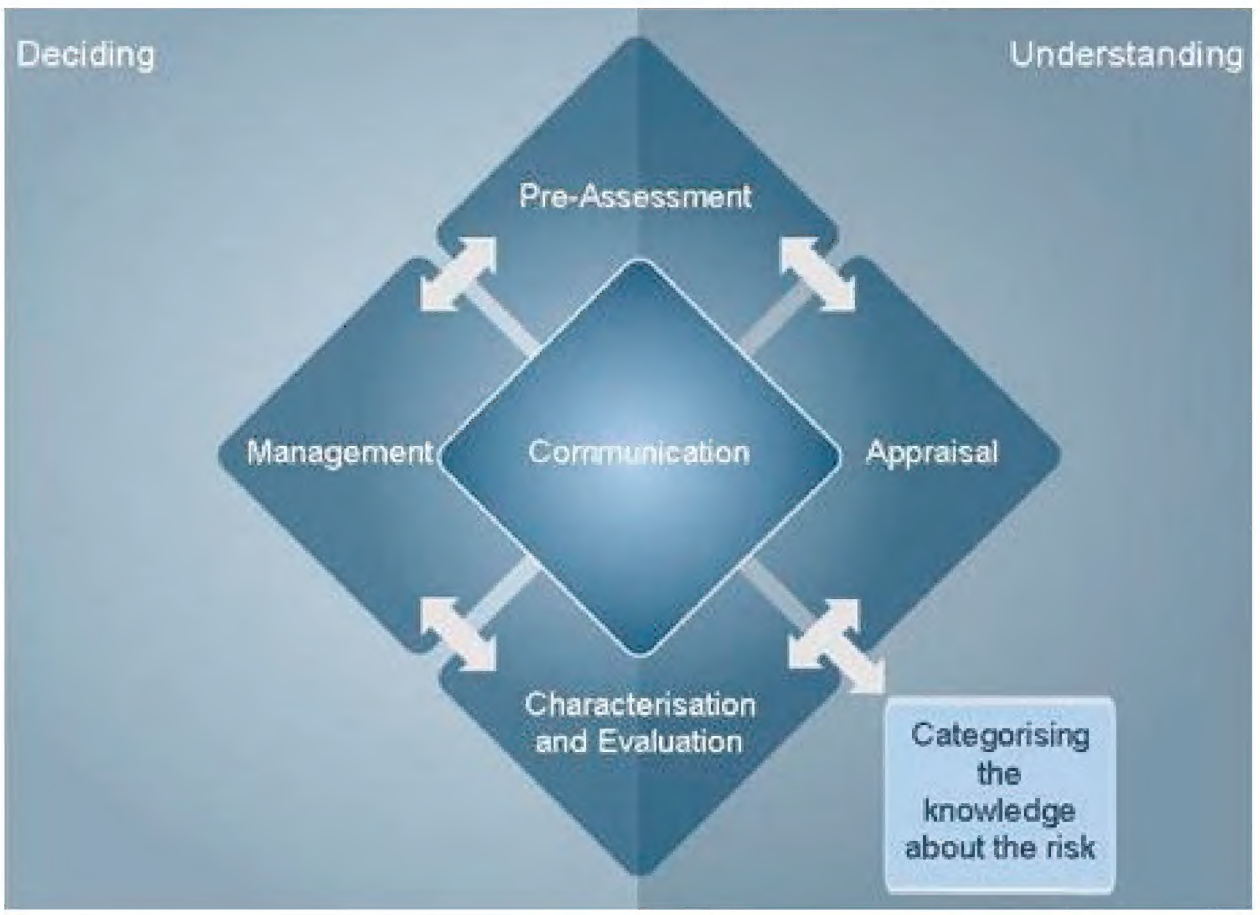

Figure 2. Biorisk governance process.

Biosafety

The World Health Organization issues a practical guidance from which the understanding of biosafety on techniques for use in laboratories is derived. The WHO Laboratory biosafety Manual (LBM) considers biosafety to be "the containment principles, technologies and practices that are implemented to prevent unintentional exposure to pathogens and toxins, or their accidental release." The LBM contains expert guidance on how to implement the relevant principles, technologies and practices. The WHO encourages all states to consider such concepts when developing and enhancing national regulatory regimes. The international guidance is then tailored to fit precise national requirements. Such concepts are consistent across public, animal and plant health sectors and close cooperation between the WHO, FAO and OIE contributes to the development of relevant guidance and understandings. Biosafety is one term that is used to describe the policies and procedures adopted to ensure the environmentally safe application of modem biotechnology (WHO 2014).

Biosecurity

The term biosecurity is more complex as it can have different meanings in different contexts. In the Biological Weapons Convention (BWC) setting, it is most commonly

used to refer to mechanisms to establish and maintain the security and oversight of pathogenic microorganisms, toxins and relevant resources. The implications of biosecurity in public health settings, however, relate more closely to the BWC. Laboratory biosecurity describes "the protection, control and accountability for valuable biological materials within laboratories, in order to prevent their unauthorized access, loss, theft, misuse, diversion or intentional release." Biosafety is one term that is used to describe the policies and procedures adopted to ensure the environmentally safe.

Finally, it is important to note that concern about risks to human health and to the environment is not peculiar to biotechnology. Rather, these questions have emerged as an important component in the development, regulation and promotion of the products of many new and older technologies such as chemicals and pharmaceuticals.

2.1 Laboratory practices

2.1.1 Personal protective equipment

Personal protective equipment (PPE) is an essential element laboratory safety, and must be provided to all staff members by their respective institutions free of charge. PPE provided to staff members includes, but is not limited to:

- Gloves
- Disposable or reusable laboratory coats (impervious to liquids)
- Side shields (for glasses)
- Face shields
- Surgical masks
- Safety glasses
- Prescription safety glasses
- Goggles
- Hoods
- Shoe covers
- Respiratory protection (e.g., N95 respirator)
- Other site-specific PPE

At a minimum, laboratory personnel shall wear gloves and a laboratory coat whenever handling biological agents, cells and tissues. Safety glasses with side shields, goggles, or face shield shall be worn when these materials could potentially be splashed in the face. Laboratory personnel shall wear other personal protective equipment (apron, face shield, surgical mask, N95 respirator, etc.) as needed or required to prevent potentially infectious materials from reaching their clothes, skin, eyes, mouth, or other mucous membranes. PPE must be removed prior to leaving the work area and placed in designated areas. PPE must be treated as medical waste when discarded. If PPE is not disposable, PPE shall be cleaned with disinfectant before and after use or laundered by an outside vendor by placing it into designated biohazard bags provided by the vendor.

2.1.2 Biological safety cabinets

Biological safety cabinets (BSCs) provide a primary level of containment for working safely with potentially hazardous biological materials. When combined with standard microbiological practices, BSCs can protect both laboratory personnel and the environment. Although many may think that the principle function of BSCs is to protect cells and cultures from contamination by bacteria and fungi, their primary purpose should be to protect the laboratory workers and the environment from exposures to potentially infectious agents.

BSCs are designated as Class I, II, or III based on specific airflow patterns within the BSC and on the locations of high efficiency particulate air (HEPA) filters within the unit. HEPA filters are usually composed of a pleated sheet of borosilicate fiber material that has been treated with a wet-strength water-repellant binder. These filters are specifically designed to remove particles equal and greater than 0.3 microns with an efficiency of 99.97%. This filtration level will capture bacteria, spores, and viruses from the filtered air (Fig. 3).

Implementation of the following procedures will ensure optimal operation of a BSC and maintain product, personnel and environmental protection:

- Front and rear grills should be free of clutter to allow proper air intake.
- Sash should not be raised above the specified level.
- Personal protective equipment (laboratory coat or gown, gloves) must be worn in order to maintain product and personnel protection.
- Work surfaces must be disinfected before and after working in the BSC.
- Bunsen burner use will cause airflow disruptions and damage to the HEPA filter and potentially cause a fire, and should be avoided.
- Certification must be performed annually.

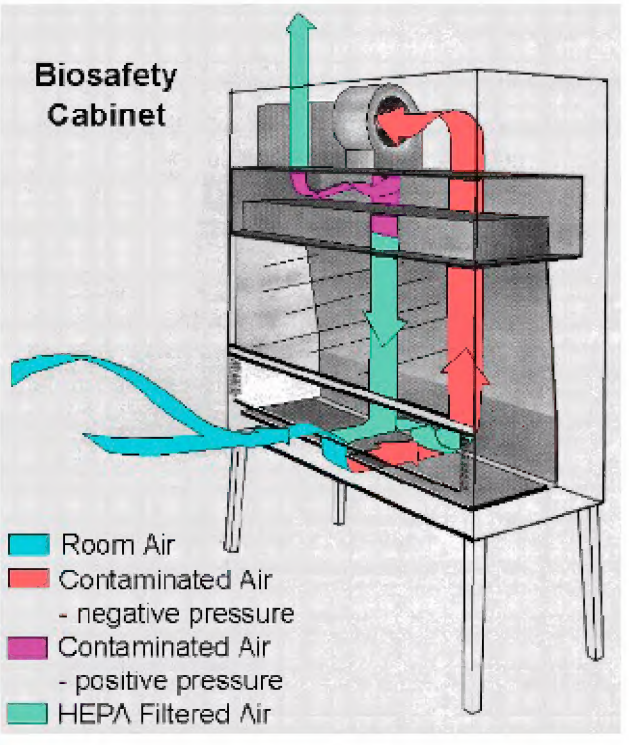

Figure 3. Airflow Pattern in Biosafety Cabinet.

BSCs are required to be tested and certified annually by technicians accredited by the National Sanitation Foundation (NSF International). Additionally, BSCs will be certified when they are first installed and whenever they are moved, even to a nearby laboratory, because the HEPA filters may be dislodged from their proper fitting during these moves.

2.1.3 Disposal of biological waste

Biological waste may be disposed of in three ways: designated biological waste box, chemical disinfection, and steam sterilization/autoclave. Appropriate disinfection procedures will be chosen and utilized in accordance with both the Principal Investigator (PI) and the Biological Safety Officer (BSO) in order to ensure adequate decontamination of biological wastes.

Infectious and potentially infectious non-sharp waste and waste containing rDNA may only be disposed of in designated biological waste boxes. Each box is labeled with the universal biohazard symbol and is lined with two red plastic bags to reduce the likelihood of leakage. When a biological waste box is between two thirds (2/3) and three-quarters (3/4) full, the two bags should be individually sealed with tape and the box itself sealed with two-inch tape. Do not overfill the boxes. Boxes that leak any liquid or that exceed 55 pounds will not be moved or removed for disposal.

Liquid biological and rDNA waste must be rendered non-infectious by steam sterilization or chemical disinfection prior to sink disposal. If chemical disinfection is selected, full-strength household chlorine bleach may be added to the waste container, such as an aspiration flask, so that the final solution concentration of bleach will be 10%. Contact time should be at least 30 minutes prior to sink disposal for bleach. Use bleach that is labeled "mercury-free".

Before disposing of the treated solution down the sink, check the pH to ensure it is within the permissible pH range. If it is within the permissible range, then disposal of the treated solution in the sink should be done with running tap water to minimize possible plumbing damage due to the corrosive effects of the disinfectants. Autoclaving solutions containing bleach is not permitted due to the potential for production of toxic chlorine gas (National Select Agent Registry, CDC 2016).

2.1.4 Biological/radionuclide waste

Biological/Radionuclide Waste, disinfect the infectious material with chemical disinfectant and dispose of as chemical waste. Select chemical disinfectants carefully because some disinfectants can react with chemicals.

2.1.5 Sharps management

Some of the most serious accidents in biological laboratories are those caused by puncture wounds through skin (percutaneous exposures). All objects that can puncture skin

are designated as sharps and require special disposal treatment. Examples of sharps include hypodermic needles, glass Pasteur pipettes, razor blades, broken glass and suture needles. Sharps must be disposed of separately from all other waste streams and sharps containers cannot be disposed of with other biological waste. Federal regulations concerning sharps primarily focus on work with human bodily fluids. Research work conducted with animals only is not required to utilize engineered safety sharps; however, it is recommended that engineered devices be used whenever practical. Because the majority of laboratory biohazard injuries are due to hypodermic needles, special attention has focused on their use and disposal. Some guidelines include:

- Minimize use of needles and syringes.
- Do not bend, shear, or break needles.
- Do not recap needles.
- Do not remove needles from syringes.
- Dispose of the entire syringe-needle combination in a sharps container.
- Be careful during cleanup; some sharp items may be hidden in the waste materials.
- If a needle stick occurs, encourage the wound to bleed for a few minutes, wash the area, and then get medical attention immediately. In 2001, in response to the Needle stick Safety and Prevention Act, OSHA revised the BBP Standard 29 CFR 1910.1030.

2.1.5.1 Sharps disposal

To prevent injury from sharps, place all needles, Pasteur pipettes, syringes, suture needles, scalpels, and razor blades into standard sharps containers. Large volumetric/serological pipettes, or other items that can puncture the biological waste red bags should be disposed of in Sharps containers. Sharps containers must be red, fluorescent orange or orange-red leak proof, rigid, puncture-resistant, shatterproof containers that that are marked prominently with the universal biohazard warning symbol and the word "Biohazard" in a contrasting color. Place sharps containers in convenient locations near work areas so they will be used. Do not overfill the sharps containers. Containers should be sealed when they are three-quarters (3/4) full.

2.1.5.2 Broken and clean glassware disposal

Place clean glassware into the standard recycling boxes for glassware. Contaminated broken test tubes or other broken glass items must be placed directly into sharps containers.

2.1.5.3 Pasteur pipettes disposal

Pasteur pipettes are a special case because Massachusetts law requires that they be considered as a sharps waste no matter what their previous use. Discard glass Pasteur pipettes directly into sharps containers; do not use broken glassware boxes. Plastic pipettes and serological pipettes that could puncture the red waste bags should also be disposed of in sharps containers.

2.1.6 Disinfection and decontamination

Disinfection and decontamination are terms that are often used interchangeably, but they each have specific definitions. Disinfection is a chemical or physical treatment that destroys most biological agents, except spores. Decontamination refers to a chemical or physical treatment that destroys most biological agents to a low level, but not necessarily zero. A number of disinfectants are commonly used in laboratory settings, particularly to wipe down surfaces to remove infectious agents.

2.1.6.1 Autoclaving procedures

Autoclaves work by denaturing biological molecules with superheated steam; dry heat is not nearly as effective. For example, it takes 12 minutes to kill most spores with steam at 121 degrees Celsius (°C), while 6 hours are required with dry heat at the same temperature. It is the steam that kills.

As a result, anything that does not come in contact with steam inside the autoclave may not be adequately decontaminated. The potential for inadequate decontamination becomes a greater concern when sealed biohazard bags are placed in an autoclave. There are two simple solutions:

1. carefully cut open the bag, or
2. place about 200 milliliters of water in the bag before sealing. Typically, bags (24" x 36") of solid plastic waste take from 45 minutes to 1 hour to reach sterilizing temperatures throughout its contents.

2.1.6.2 Autoclave testing and validation

Autoclaves should be tested quarterly and validated to insure that they are operating properly and killing the biological organisms in each autoclave load. The preferred method for autoclave validation is to test it with a commercial spore test system. This system uses ampoules containing a bacterial species called *Bacillus stearothermophilus* that is tolerant to high temperatures and contains a color indicator solution. The ampoules are autoclaved under realistic conditions, such as in the middle of a bag of waste, and then incubated for two days at 56°C. If the spores grow, a color change will occur indicating inadequate sterilization in the autoclave. If there is no growth, no color change occurs and the autoclaving procedure is adequate. Frequent validation is not necessary, unless required by regulatory authorities in special circumstances. By using an established autoclave test procedure, quarterly checks with a biological indicator usually adequate to assure proper autoclave function and to detect gradual deterioration of operation. It is important to note that autoclave tape indicates only that a critical temperature was reached; it does not indicate the length of time at the desired temperature or whether steam was present.

The following tips will help prevent injury and property damage when using the autoclave.

- Do not overfill containers. Leave the top third as empty expansion space.
- Use only vented closures so that steam may enter the load.
- Place contaminated materials in autoclave bags. Place bags inside plastic or metal trays when autoclaving.
- Use only containers designed for sterilization. Use plastic or metal trays.
- When opening the autoclave, wear appropriate PPE as items may be hot to the touch.

2.1.7 Spill management

Management of Small Spills (spills 100 ml)

The following procedures are recommended for a large volume biological spill in the laboratory area, in a BSC, or if equipment malfunctions while processing biological materials:

- If the spill occurs in a BSC, close the sash and leave the BSC running.
- Keep people out of the area to prevent spread of the contamination. Put up a warning sign indicating that there was a spill in the BSC, the steps taken to treat/contain the spill, and contact information for a responsibly party.
- Remove any contaminated clothing and put it into a biohazard bag for decontamination later.
- Wash hands and exposed skin thoroughly with soap and water.

3. Biorisk assessment

Risk assessment is the backbone of the practice of biosafety. While there are many tools available to assist in the assessment of risk for a given procedure or experiment, the most important component is professional judgment. Risk assessments should be based on the specific characteristics of the organisms being considered for use, the equipment and procedures to be employed, animal models that may be used, and the containment equipment and facilities available. The performed risk assessments should be reviewed routinely and revised when necessary, taking into consideration the acquisition of new data having a bearing on the degree of risk and other relevant new information from the scientific literature. One of the most helpful tools available for performing a microbiological risk assessment is the listing of risk groups for microbiological agents. However, simple reference to the risk grouping for a particular agent is insufficient in the conduct of a risk assessment. Other factors that should be considered, as appropriate, include:

1. Pathogenicity of the agent and infectious dose
2. Potential outcome of exposure
3. Natural route of infection

4. Other routes of infection, resulting from laboratory manipulations (parenteral, airborne, ingestion)
5. Stability of the agent in the environment
6. Concentration of the agent and volume of concentrated material to be manipulated
7. Presence of a suitable host (human or animal)
8. Information available from animal studies and reports of laboratory-acquired infections or clinical reports
9. Laboratory activity planned (sonication, aerosolization, centrifugation, etc.)
10. Any genetic manipulation of the organism that may extend the host range of the agent or alter the agent's sensitivity to known, effective treatment regimens
11. Local availability of effective prophylaxis or therapeutic interventions

4. The laboratory biorisk management approach

Laboratory biorisk management is fundamentally a culture of rigorously assessing risks, deciding how to mitigate those risks deemed to be unacceptable and establishing mechanisms to constantly evaluate the effectiveness of the control measures.

4.1 Hazard Analysis

In order to determine which practices and procedures are required when working with biological materials, a risk assessment should be conducted. Based on an agent-based biorisk assessment that includes laboratory biosecurity considerations, laboratories containing Valuable Biological Materials (VBM) should develop systems and controls to provide the required degree of assurance that biosafety and laboratory biosecurity risks are appropriately managed, and that the consequences of release of any VBM from the laboratory are appropriately minimized. (http://www.biosecurity.sandia.gov/BioRAM/Biorisk%20Framework%20Report.pdf)

Managing these risks represents:

1. Reducing the risk of unintentional exposure to pathogens and toxins or their accidental release (biosafety), and reducing the risk of unauthorized access, loss, theft, misuse, diversion or intentional release of VBM to tolerable, acceptable levels (laboratory biosecurity).
2. Providing assurance, internally and externally (facility, local area, government, global community, etc.), that suitable measures have been adopted and effectively implemented.
3. Providing a framework for continuous awareness-raising for biosafety, laboratory biosecurity and ethical code of conduct, and training within the facility.

The present document does not provide prescriptive guidance on the development of laboratory biosecurity measures, but describes recommendations and performance expectations, placing responsibility on national authorities and facility managers to demonstrate that appropriate and reasoned biorisk minimization procedures have been established and will be implemented. These recommendations do not call for compliance with a set of requirements, but rather help to identify and set goals to be achieved. This approach allows countries and facility managers to define and choose appropriate systems and controls to ensure that the biorisk management goals that have been identified are reached. It allows institutions to adapt their laboratory biosecurity plans to their particular situation.

4.2 Securing valuable biological materials (VBM)

Laboratory biosecurity is more than just the safeguarding of dangerous pathogens and toxins from individuals or organizations who would use them for harm. While protection of dangerous pathogens and toxins is obviously appropriate, the scientific, medical and pharmaceutical communities should also consider protecting materials with historical, medical, epidemiological, commercial or scientific value. These decisions should be taken with due consideration to the fact that scientists serve only as temporary custodians of valuable scientific assets whose past and current value to science may be understood, but whose utility for the future can only be estimated.

Some VBM have intrinsic value and they need to be preserved for study by future generations of scientists. Their transfer and sharing should be encouraged or maintained as long as appropriate documentation allowing to track them is available. Thus scientists have a duty to maintain VBM according to current best practice. If a decision is taken to destroy unwanted or unnecessary materials, protocols must be followed to ensure their full and complete destruction and documentation. The protection of VBM includes appropriate storage conditions, documentation of their storage, use, transfer to more appropriate laboratories, or proof of complete destruction.

The classification of biological materials as VBM should be left to their caretakers (laboratory managers and scientists) who should know and understand their value and should be able to address and define the level of protection required. To address these issues, the caretakers of VBM should consult with partners, e.g. in the research community and in the security, intelligence or information technology (IT) sectors to ensure the protection of their valuable assets against identified biorisks. If the facility holding the collection cannot ensure its protection, the laboratory manager together with the responsible scientist(s) should make arrangements to safely transfer them to a more secure site. In this way, policy-makers, scientists, laboratory directors and security engineers, supported by journal editors and publishers of research results, may achieve an appropriate balance between the protection of VBM and the preservation of an environment that promotes legitimate microbiological research.

All microorganisms, natural or laboratory-modified, may be included in the broad definition of VBM. Although some agents have heightened capacities to cause harm if intentionally misused, virtually all may have legitimate uses for medical, commercial and scientific applications. Their value should prompt a responsibility to limit opportunities for VBM to be inappropriately accessed while at the same time preserve opportunities for their study and legitimate use, e.g. for the development of improved vaccines, diagnostics and therapies, work that requires handling, using, transporting, transferring and sharing of VBM.

5. Guidelines for basic level laboratories

A very specialized research laboratory that deals with infectious agents is the biosafety lab. Whether performing research or production activities, when working with infectious materials, organisms or perhaps even laboratory animals, the proper degree of protection is of utmost importance. Protection for laboratory personnel, the environment and the local community must be considered and ensured. Biological safety levels are ranked from one to four and are selected based on the biological agents or organisms, work practices, safety equipment and facility design on which the research or work is being conducted. Each level up builds on the previous level, adding constraints and barriers (http://www.cdc.gov/biosafety/). (Table 1)

The four biosafety levels were developed to protect against a world of select agents. These agents include bacteria, fungi, parasites, prions, rickettsial agents and viruses, the latter being probably the largest and most important group. In many instances the work or research involves vertebrate animals, everything from mice to cattle. When vertebrates are involved, additional precautions and safety requirements are necessary. Using the most infectious agents also means extensive security measures are in place, not only because of their virulence but also because of their potential for use in bioterrorism.

5.1 Biosafety level laboratories

5.1.1 Biosafety level 1

Biosafety level one, the lowest level, applies to work with agents that usually pose a minimal potential threat to laboratory workers and the environment and do not consistently cause disease in healthy adults. Research with these agents is generally performed on standard open laboratory benches without the use of special containment equipment. BSL 1 labs are not usually isolated from the general building. Training on the specific procedures is given to the lab personnel, who are supervised by a trained microbiologist or scientist. Standard microbiology practices are usually enough to protect laboratory workers and other employees in the building.

Table 1. Description of biosafety level laboratories.

Biosafety level	BSL-1	BSL-2	BSL-3	BSL-4
Description	• No Contamination • Defined Organisms • Unlikely to cause disease	• Containment • Moderate Risk • Disease of varying severity	• High Containment • Aerosol Transmission • Serious/potentially lethal disease	• Max Containment • "Exotic", High-Risk Agents • Life-threatening disease
Sample organisms	*E.coli*	Influenza, HIV, Lyme Disease	Tuberculosis	Ebola Virus
Pathogen type	Agents that present minimal potential hazard to personnel and the environment	Agents associated with human disease & pose moderate hazards to personnel & the environment	Indigenous or exotic agents, agents that present a potential for aerosol transmission, & agents causing serious or potentially lethal disease.	Dangerous & exotic agents that pose a high risk of aerosol transmitted laboratory infections & life-threatening disease.
Autoclave requirements	None	None	Pass-thru autoclave with Bioseal required in laboratory room.	Pass-thru autoclave with Bioseal required in laboratory room.

The guidance and recommendations given as minimum requirements pertaining to laboratories of all biosafety levels are directed at microorganisms in Risk Groups 1–4. Although some of the precautions may appear to be unnecessary for some organisms in RiskGroup1, they are desirable for training purposes to promote good microbiological techniques (GMT).

5.1.2 Biosafety level 2

Diagnostic and health-care laboratories (public health, clinical or hospital-based) must all be designed for Biosafety Level 2 or above. As no laboratory has complete control over the specimens it receives, laboratory workers may be exposed to organisms in higher risk groups than anticipated. This possibility must be recognized in the development of safety plans and policies (https://www.eolss.net/sample-chapters/C17/E6-58-01-08.pdf).

Biosafety level two would cover work with agents associated with human disease, in other words, pathogenic or infectious organisms posing a moderate hazard. Examples are the equine encephalitis viruses and HIV when performing routine diagnostic procedures or work with clinical specimens. Therefore, because of their potential to cause human disease, great care is used to prevent percutaneous injury (needlesticks, cuts and other breaches of the skin), ingestion and mucous membrane exposures in addition to the standard microbiological practices of BSL 1. Contaminated sharps are handled with extreme caution. Use of disposable syringe-needle units and appropriate puncture-resistant sharps containers is mandatory. Direct handling of broken glassware is prohibited, and decontamination of all sharps prior to disposal is standard practice. The laboratory's written biosafety manual details any needed immunizations (e.g., hepatitis B vaccine or TB skin testing) and whether serum banking is required for at-risk lab personnel. Access to the lab is more controlled than for BSL 1 facilities.

Figure 4. Biosafety level 2.

Immuno compromised, immune suppressed and other persons with increased risk for infection may be denied admittance at the discretion of the laboratory director (Fig. 4).

BSL 2 labs must provide the next level of barriers, mainly safety equipment and facilities. Preferably biosafety cabinet, autoclave and other decontamination equipments, first aid kits and a readily available eyewash station is needed. Self closing lockable doors and biohazard warning signs are also required at all access points.

5.1.3 Biosafety level 3

The containment laboratory – Biosafety Level 3 is designed and provided for work with Risk Group 3 microorganisms and with large volumes or high concentrations of Risk Group 2 microorganisms that pose an increased risk of aerosol spread. Biosafety Level 3 containment requires the strengthening of the operational and safety programmes over and above those for basic laboratories – Biosafety Levels 1 and 2. The guidelines given above are presented in the form of additions to those for basic laboratories – Biosafety Levels 1 and 2, which must therefore be applied before those specific for the containment laboratory – Biosafety Level 3.

Yellow fever, St. Louis encephalitis and West Nile virus are examples of agents requiring biosafety level 3 practices and containment. Work with these agents is strictly controlled and must be registered with all appropriate government agencies. These are indigenous or exotic agents that may cause serious or lethal disease via aerosol transmission, i.e., simple inhalation of particles or droplets. The pathogenicity and communicability of these agents dictates the next level of protective procedures and barriers. Add to all the BSL 2 practices and equipment even more stringent access control and decontamination of all wastes, including lab clothing before laundering, within the lab

Figure 5. Biosafety level 3 laboratory.

facility. Baseline serum samples are collected from all lab and other at-risk personnel as appropriate.

More protective primary barriers are used in BSL 3 laboratories, including solid-front wraparound gowns, scrub suits or coveralls made of materials such as Tyvek® and respirators as necessary. Facility design should incorporate self-closing double-door access separated from general building corridors. The ventilation must provide ducted, directional airflow by drawing air into the lab from clean areas and with no recirculation (Fig. 5).

5.1.4 Biosafety level 4

The maximum containment laboratory – Biosafety Level 4 is designed for work with Risk Group 4 microorganisms. Before such a laboratory is constructed and put into operation, intensive consultations should be held with institutions that have had experience of operating a similar facility. Operational maximum containment laboratories – Biosafety Level 4 should be under the control of national or other appropriate health authorities (Fig. 6).

Agents requiring BSL 4 facilities and practices are extremely dangerous and pose a high risk of life-threatening disease. Examples are the Ebola virus, the Lassa virus, and any agent with unknown risks of pathogenicity and transmission. These facilities provide the maximum protection and containment. To the BSL 3 practices, we add requirements for complete clothing change before entry, a shower on exit and decontamination of all materials prior to leaving the facility.

Figure 6. Biosafety level 4 laboratory.

The BSL 4 laboratory should contain a Class III biological safety cabinet but may use a Class I or II BSC in combination with a positive-pressure, air-supplied full-body suit. Usually, BSL 4 laboratories are in separate buildings or a totally isolated zone with dedicated supply and exhaust ventilation. Exhaust streams are filtered through high-efficiency particulate air (HEPA) filters, depending on the agents used. Along with those such as impervious, easy-to-clean surfaces, insect and rodent control, and total barrier sealing of all wall, floor and ceiling penetrations has to be paid attention.

5.2 Facility commissioning

Laboratory/facility commissioning may be defined as the systematic review and documentation process signifying that specified laboratory structural components, systems and/or system components have been installed, inspected, functionally tested and verified to meet national or international standards, as appropriate. The respective building system's design criteria and design function establish these requirements. In other words, laboratories designated as Biosafety Levels 1–4 will have different and increasingly complex commissioning requirements. Geographical and climatic conditions, such as geological fault lines or extreme heat, cold or humidity may also affect the laboratory design and therefore the commissioning requirements. Upon the completion of the commissioning process, the pertinent structural components and support systems will have been subjected to the various operating conditions and failure modes that can be reasonably expected, and will have been approved. The commissioning process and acceptance criteria should be established early, preferably during the programming phase

of the construction or renovation project. By acknowledging the commissioning process early in the project, architects, engineers, safety and health personnel and ultimately the laboratory occupants understand the performance requirements of the specific laboratory and set uniform expectations for laboratory and/or facility performance. The commissioning process provides the institution and the surrounding community with a greater degree of confidence that the structural, electrical, mechanical and plumbing systems, containment and decontamination systems, and security and alarm systems will operate as designed, to assure containment of any potentially dangerous microorganisms being worked with in a particular laboratory or animal facility. Commissioning activities generally begin during the programming phase of the project and proceed through the construction and subsequent warranty period for the laboratory/facility. Warranty periods should generally extend for one year following occupancy. It is recommended that a commissioning agent is retained who is independent of the architectural, engineering and construction firms involved in the design and construction. The commissioning agent serves as an advocate for the institution constructing or renovating the laboratory and should be considered as a member of the design team; involvement of the agent in the early programming phase of the project is essential. In some cases, the institution may act as its own commissioning agent. In the case of more complex laboratory facilities (Biosafety Levels 3 or 4), the institution may wish to retain an outside commissioning agent who has demonstrated experience and success in the commissioning of complex biosafety laboratory and animal facilities. When an independent commissioning agent is used, the institution should still be a member of the commissioning team.

5.3. Facility certification

The laboratory biorisk management standard CWA 15793, which is based on a management system approach like ISO 9001, ISO 14001 or OHSAS 18001, is intended to help laboratories develop a systematic framework for managing their risks. First, it requires a policy statement, which puts forth a strategic positioning and a formal commitment from the organization's top management. Secondly, biosecurity is included in the whole risk management approach together with biosafety. Last but not least, the planning phase is not limited to the risk assessment, but also includes planning for the resources needed for the implementation of the decisions and the monitoring of their outcome, which appears as some guarantee for a sustainable management. In general, key features of all management systems include structuring the system to achieve the organization's objectives in the most effective and efficient way, understanding the interdependencies between the processes of the system, structuring approaches to harmonize and integrate processes, providing a better understanding of the roles and responsibilities necessary for achieving common objectives (and reducing cross-functional barriers), understanding organizational capabilities and establishing resource constraints prior to action, targeting and defining how specific activities within a system should operate, and continually improving the system through meas-

urement and evaluation. All of these management system elements are applicable to managing laboratory biorisks and their implementation can be enhanced through a risk governance framework.

6. Safety organization and training

It is essential that each laboratory organization has a comprehensive safety policy, a safety manual, and supporting programmes for their implementation. The responsibility for this normally rests with the director or head of the institute or laboratory, who may delegate certain duties to a biosafety officer or other appropriate personnel. Laboratory safety is also the responsibility of all supervisors and laboratory employees, and individual workers are responsible for their own safety and that of their colleagues. Employees are expected to perform their work safely and should report any unsafe acts, conditions or incidents to their supervisor. Periodic safety audits by internal or external personnel are desirable (Rodney K. Wilson 2015).

6.1 Biosafety officer

Wherever possible a biosafety officer should be appointed to ensure that biosafety policies and programmes are followed consistently throughout the laboratory. The biosafety officer executes these duties on behalf of the head of the institute or laboratory. In small units, the biosafety officer may be a microbiologist or a member of the technical staff, who may perform these duties on a defined part-time basis. Whatever the degree of involvement in biosafety, the person designated should possess the professional competence necessary to suggest, review and approve specific activities that follow appropriate biocontainment and biosafety procedures. The biosafety officer should apply relevant national and international rules, regulations and guidelines, as well as assist the laboratory in developing standard operating procedures. The person appointed must have a technical background in microbiology, biochemistry and basic physical and biological sciences. Knowledge of laboratory and clinical practices and safety, including containment equipment, and engineering principles relevant to the design, operation and maintenance of facilities is highly desirable. The biosafety officer should also be able to communicate effectively with administrative, technical and support personnel.

6.2 Biosafety committee

Biosafety committee a biosafety committee should be constituted to develop institutional biosafety policies and codes of practice. The biosafety committee should also review research protocols for work involving infectious agents, animal use, recombinant DNA and genetically modified materials. Other functions of the committee may

include risk assessments, formulation of new safety policies and arbitration in disputes over safety matters. The membership of the biosafety committee should reflect the diverse occupational areas of the organization as well as its scientific expertise (https://bch.cbd.int/database/attachment/?id=10858). The composition of a basic biosafety committee may include:

- Biosafety officer(s)
- Scientists
- Medical personnel
- Veterinarian(s) (if work with animals is conducted)
- Representatives of technical staff
- Representatives of laboratory management.

The biosafety committee should seek advice from different departmental and specialist safety officers (e.g. with expertise in radiation protection, industrial safety, fire prevention, etc.) and may at times require assistance from independent experts in various associated fields, local authorities and national regulatory bodies. Community members may also be helpful if there is a particularly contentious or sensitive protocol under discussion.

7. Organizations Monitoring Biorisk

7. 1 World Health Organization (WHO)

http://www.who.int/csr/bioriskreduction

The WHO has at least two sets of relevant activities: the Biosafety and Laboratory Biosecurity Programme; and the project of the biorisk reduction for dangerous pathogens team on life science research and development for global health security.

The WHO Biosafety and Laboratory Biosecurity programme is designed to assist member states understand, adopt and implement biorisk management strategies to minimize risks of infections through safe and secure practices in laboratory and transport environments, and to accomplish these goals in a cost-effective manner. It is part of WHO's efforts to establish a biosafety and laboratory biosecurity culture worldwide. To this end, the programme provides guidance on, and promotes the use of, safe and secure workplace practices, appropriate protective equipment, engineering and administrative controls in the handling of pathogenic organisms in laboratories, during transportation, in field investigations and in vaccine manufacturing facilities, to protect workers, the environment and the community from exposure, infection, and subsequent development of disease. Five WHO biosafety collaborating centres support the Global Biosafety and Laboratory Biosecurity Programme. They each have nominated a focal point to be a member of the WHO Biosafety Advisory Group (BAG) to support the programme. The BAG meets regularly to address outstanding biosafety and laboratory biosecurity issues, to discuss activities, projects and collaborations.

7.2 Food and Agriculture Organization (FAO)

http://www.fao.org/biosecurity

The activities of FAO are not so obviously linked to the topics under discussion at the Biological Weapons Convention (BWC) meeting of experts. Nevertheless, certain elements, especially as they relate to the development of biosafety best practices, are closely related; others contain resources which could be extrapolated to fit the BWC context, such as principles of capacity building in disease-related fields. The FAO has conducted a technical consultation on biological risk management in food and agriculture in Thailand in 2003; created an international portal on food safety, animal and plant health; established a Working Group on Biosafety; detailed examples of national approaches to biosecurity; conducts a capacity building programme; and has reviewed certain thematic areas, including biotechnology in food and agriculture, biotechnology and food safety, and animal and plant health.

7.3 World Organization for Animal Health (OIE)

http://www.oie.int

The OIE collaborates with other international organisations on the development of generic biosafety and safe transport guidance, the OIE produces a number of key documents specifically targeting animal-related fields. The OIE produces the international health standards for animals and animal products – trade standards and biological standards: the Terrestrial Animal Health Code; the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals; the Aquatic Animal Health Code; and the Manual of Diagnostic Tests for Aquatic Animals. These standards deal with a range of pertinent issues: risk management approaches and principles; biosecurity consideration (especially in the animal and agricultural use of the term); identification and traceability of live animals; hygiene precautions; and disinfection and disinsectisation.

The OIE also produces a number of other resources. The OIE Quality Standard and Guidelines for Veterinary Laboratories: Infectious Diseases sets out the management and technical competence for the accreditation of testing for infectious animal disease. This quality control system contributes to ensuring the safe and secure operation of relevant facilities. The standards cover: management requirements (including quality systems, document control, records, internal audits and management reviews); technical requirements (including personnel issues, equipment, measurement traceability and handling of specimens); validation of laboratory techniques; and international reference standards.

8. Conclusion

Some of the most worrisome incidents happen in laboratory due to overlooking of safety rules and not following the guidelines given by Instructors/ safety trainers. Bad

handling of instruments and chemicals without reading safety guidelines, misusing them for alternate purposes could cause devastation. Wearing protections and taking safety measures like how to use first aid kit, safety equipment, know the locations of the fire extinguishers, eyewash, and water taps is essential. Conducting experiments in right environment like fume hood, safety cabins, handling chemical leftovers, potential pathogens in an appropriate manner, avoid self contaminating, keeping track of harmful chemicals and strains is important. (https://wyss.harvard.edu/staticfiles/pdf/WyssBiosafetyManual-July2012.pdf)

The biorisk management approach described is composed of a biosafety, a laboratory biosecurity and an ethical component. It offers laboratory facilities a programme that should help them to protect their valuable scientific assets. Concurrently with the work of other agencies and entities that have addressed biosecurity issues in a variety of contexts and from other viewpoints, this document has addressed VBM and the growing advances in life sciences and related technologies that are likely to alter the spectrum of current and future biorisks, presenting ways to identify, prevent and minimize them. Under the ultimate responsibility of laboratory directors whose tasks should include the ability to demonstrate that risks are appropriately managed, biorisk management programmes may be divided into seven main components:

1. Identify VBM that require protection on the basis of regularly performed biorisk assessments.
2. Establish clear guidance, roles, responsibilities and authorities for those who work with or have access to VBM and to the facilities that contain them.
3. Promote a culture of awareness, shared sense of responsibility, ethics, and respect of codes of conduct within the international life science community.
4. Develop policies that do not hinder the efficient sharing of reference materials and scientific data, clinical and epidemiological specimens and related information, and that do not impede the conduct of legitimate research.
5. Strengthen collaboration between the scientific, technical and security sectors.
6. Provide appropriate training to employees of laboratory facilities.
7. Strengthen emergency response and recovery plans on the assumption that biorisk management systems can only minimize, but never really eliminate, every conceivable threat.

The threat of chemical weapons or malicious use of chemicals was always there, along with that by using advances in biotechnology microorganisms can be created against humans, livestock, crops, food, water infrastructure and other economically valuable entities (Smith et al. 2017). It is important to create a biorisk checklist to make the people aware of biohazard materials (Naroeni et al. 2016). In order to implement technologies at the laboratory working level, a management team should be created whose role is to protect workers, the environment, the product and the biological pathogen. To face the increasing biological threat from emerging infectious diseases and bioterrorism, it has become essential for governments around the globe to increase awareness and preparedness for identifying and containing those agents (Zaki 2010).

National and international monitoring authorities should prevent the proliferation and the use of chemical, biological, radiological, and nuclear (CBRN) weapons (Al Jewari and Koblentz 2016). It is urgent to realize the concept of biological risk assessment and management on handling pathogenic biological agents (PBA). The development of a methodology to assess laboratory biological risks assures the handling of PBA (Dobrokhotskiĭ and Kolombet 2010). Russia and many European Union countries were implemented international standards (CWA 15793:2008, CWA 15793:2011) in laboratory biorisk management (Dobrokhotskiĭ and Diatlov 2013, Sundqvist et al. 2013, Dobrokhotskiĭ et al. 2012). In developing countries awareness programs are necessary on biosafety/ biosecurity/ biocontainments. Technology transfer is crucial to achieve sustained scientific growth and build cooperation between countries. Programs such as seminars, conferences, workshops, policy documents related to biorisk management in biomedical and biotechnology laboratories are needed to create awareness among scientists (Khan et al. 2016).

Furthermore, the commitment to constantly improve biorisk management performance for a facility and its operation through attainable goal-setting and actual goal-achieving should be encouraged and acknowledged at all levels. Ethical, legal and economic framework conditions changes from country to country (Hamill 2017). The World Health Organization has recognized the importance of Human genetic variation both within and among population. The levels of biosafety standards differ as biological-risk assessment varies (Reymond et al. 2002).

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